Editorials

A New Design for WJM

WITH THIS ISSUE the journal enters its 10th year under the title THE WESTERN JOURNAL OF MEDICINE and its 81st year of continuous publication, under a succession of titles.

Much of THE WESTERN JOURNAL OF MEDICINE's physical appearance was inherited from its immediate predecessor, *California Medicine*. The Epitomes section, for example, has been graphically the same since its introduction 13 years ago. The layout and design for Case Reports was established 14 years ago. The journal's cover has followed the same basic single-column index format for 20 years. Moreover, other features, added at other times, have reflected the design styles of their particular periods.

In short, during the growth and improvement of the journal its graphics became increasingly inconsistent. In fact, it came to comprise so many different styles of headings and page layouts that one almost could have used an average issue to illustrate the recent history of medical journal design.

THE WESTERN JOURNAL OF MEDICINE now is the official scientific publication of seven western state medical associations. In addition, five western scientific societies have just affiliated with the journal. The circulation has reached some 47,000. With all of these factors in mind, the time seemed appropriate to take an objective look at the journal's appearance. This has been done and after some months of deliberation, development of design criteria and reviews of numerous design proposals, the results are embodied in the present issue. We hope our readers approve. —MSMW

Therapeutic Plasma Exchange: A Healthy Dose of Skepticism

AN APHORISM ATTRIBUTED to Sir William Osler asserts, "One should treat as many patients as possible with a new drug while it still has the power to heal." In the case of therapeutic plasma exchange, the medical community has embraced this tongue-in-cheek admonition with a singular enthusiasm. An estimated 50,000 therapeutic apheresis procedures were done in the United States in 1981 and about 3,000 more were carried out in Canada. Europe and Japan, with a head start in applying membrane and hollow fiber filtration techniques, seem determined to equal or surpass these figures. More than 50 different diseases have been treated by plasma exchange and future application seems to be limited only by patient availability and by physicians' imagination.

The term "plasmaphaeresis" was coined at the beginning of this century.[1] Its root is a Greek verb meaning to take away or withdraw and refers to the separation of plasma from whole blood with the return to the donor—originally dogs—of the sedimented blood cells in a resuspending medium. Early human applications involved the manual removal of plasma that contained paraproteins from patients suffering the effects of hyperviscosity from macroglobulinemia. When small amounts of plasma were removed and replaced with crystalloid solutions, plasma viscosity could be lowered significantly. No controlled trials were required to show clinical improvement.

The current therapeutic procedure, more accurately called "partial plasma exchange," or "plasma exchange" for short, is the by-product of a technology developed for an entirely different purpose. Blood cell separators were originally designed to collect large numbers of platelets and granulocytes from normal blood donors for transfusion. These instruments proved capable of exchanging liter volumes of plasma and therefore of depleting the circulation of numerous soluble factors, including immunoglobulins, lipoproteins, immune complexes and metabolic intermediates associated with a variety of disease processes. A 3- to 4-liter plasma exchange is now a technically uncomplicated procedure. It can be repeated several times a week if necessary and, depending on the rates of synthesis and degradation, can rapidly reduce the particular plasma constituent up to 70 percent.

The major questions relating to therapeutic plasma exchange remain scientific ones; these are the same questions posed by Robert Burton[2] more than 300 years ago: "In letting of blood three main circumstances are to be considered, 'who, how much, when.' " In considering the "who," one should also ask whether plasma exchange modifies the course of the underlying disease, provides only symptomatic relief, is merely a mechanical placebo or, in fact, causes some degree of harm. Even when the procedure is of proved effectiveness, physician and patient must weigh the degree of benefit against the rigors of the therapy. Does a modest decrease in morning stiffness justify semiweekly plasma exchange with the attendant risks, discomforts and expense?

Little evidence supports a role for plasma exchange as the primary form of therapy for any disease. Despite the recent spate of enthusiastic reports, there is a surprising consensus among experts that plasma

exchange represents adjunctive therapy for a select number of disorders; the indications for exchange and the supporting evidence are well summarized in the review article in this issue. The major medical controversies involve the following: (1) potential applications of plasma exchange to a wider range of conditions, especially for disorders where the pathophysiology is obscure and conventional therapy is either suboptimal or ineffective, and (2) the degree to which rigorous clinical trials are necessary to establish clinical efficacy.

The "how much" and "when" of plasma exchange are intimately related to the rationale for undertaking therapy. When a causative agent is recognized, for example, the paraprotein in macroglobulinemia, a therapeutic regimen can be designed to reduce it to an acceptable concentration. Still, variables such as concomitant drug therapy and the nature of the replacement solution may alter the synthesis, catabolism and distribution of plasma substances and may be critical determinants of the volume and frequency of treatment. These aspects of plasma exchange therapy have not been well studied. In diseases of unknown origin, objective therapeutic guides are rarely available. Yet depletions of complement components, rheumatoid factor and immune complexes, among other substances, are commonly cited as evidence that plasma exchange is effective therapy. Such substances may have no obvious relation to the cause or activity of the disease and their measurement is more appropriate for establishing machine efficiency than for determining the effectiveness of therapy.

When laboratory determinants of disease response are not available, physicians must depend on their clinical impressions of therapeutic effectiveness, notoriously unreliable in diseases of relapsing and remitting nature, especially in a small series of patients. Whereas large, randomized, prospective trials were not necessary to show the value of the use of plasmapheresis in macroglobulinemia, penicillin in pneumoccocal pneumonia or insulin in diabetes mellitus, these examples represent the exceptions rather than the rule. A 30 percent to 40 percent placebo effect is associated with most new therapies.[3] Foulds[4] reported that 80 percent of the uncontrolled trials in the literature show any given treatment to be effective, whereas only 25 percent of the randomized, controlled trials find the same treatment to be beneficial. Strikingly similar is a recent comparison of historical controls with randomized controls in six different therapies; 79 percent of the trials with historical controls reported therapy superior to control, whereas only 20 percent of randomized control trials could show efficacy.[5]

Such studies underline the unconscious bias that may distort a trial and emphasize how critical are careful selection and management of control groups in determining the outcome of a given clinical trial. In the case of plasma exchange, this may involve large, expensive, controlled clinical trials with "sham" treatment groups. Despite heated controversy, the National Institutes of Health and several university centers have adopted this approach as the most reasonable way to determine the true value of therapeutic plasma exchange. The Canadian government has established the Canadian National Plasma Exchange Study Group to conduct prospective controlled trials and will likely establish national therapeutic guidelines based on the outcome of these studies. Third-party insurers, among others, will be watching these studies with great interest.

Financial concerns have surfaced within the medical community, the federal government, private insurers and various consumer groups. While the economic issues are significant, it is likely that technology can substantially reduce the costs of plasma exchange should the scientific results provide the impetus to do so. Currently, in addition to personnel time, a plasma exchange involves the use of a $30,000 instrument and several hundred dollars' worth of disposable plastic supplies and replacement fluids. When procedure fees, professional fees, pharmacy fees and laboratory fees are totaled, the cost per procedure frequently exceeds $1,000. Reimbursement is sometimes contingent on being admitted to hospital for treatment, so that unnecessary hospital costs may be generated as well. On the brighter side, a new generation of instruments, specifically designed for plasma exchange, has been introduced. Based on filtration techniques, these instruments can potentially remove a more selective fraction of plasma and obviate the need for expensive replacement fluids. Even more specific are a variety of affinity columns already under evaluation in selected clinical situations. Once the principles of effective therapeutic exchange are better understood, the cost per procedure should drop substantially.

Whereas the list of potential complications is extensive, the risks of plasma exchange are small. Most adverse reactions are mild and related to allergies or volume changes. When plasma is used as a replacement fluid, the further risk of transfusion-transmitted diseases is introduced. Yet only 35 deaths associated with therapeutic apheresis have been discovered in a recent worldwide survey and several of these were more likely coincidental than causally related to the procedure. Although accurate figures for the number of procedures done in the same period are not available, when plasma exchange is carried out by experienced personnel, the mortality must be vanishingly small.

Therapeutic plasma exchange remains primarily an investigational procedure. The preliminary animal experiments of Abel and associates moved them to write:

> If this method can be employed without harmful consequences, it is probable that it could be applied in a bolder manner and in a greater variety of morbid states than the time honored but often debatable venesection of medical practice. An empirical method so universally practiced since prehippocratic days almost certainly contains a basis of truth.[1]

Enthusiasts tout the virtues of plasma exchange in an increasingly bold manner. Until the "basis of truth"

has been properly tested and established, it seems prudent to approach these claims with a healthy scientific skepticism.

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The Physicians' Share of Limited Dollars for Health Care

IT IS INCREASINGLY EVIDENT that the era of virtually unlimited dollars for health care has ended. Now and for the foreseeable future the number of dollars and other resources available for health care will be limited, actually quite finite instead of essentially infinite. The problems that this will pose have yet to be fully addressed. Physicians may reasonably be concerned with what might be their appropriate share of these limited health care dollars.

Victor Fuchs has considered this problem.[1] He points out that if the dollars for health care are limited the physicians' share of these dollars must bear some relationship to the nonphysician expenditures for health care. Quite simply the greater the nonphysician expenditures, the fewer dollars are available to pay for physicians' services. If this is true, it is clearly in the economic self-interest of physicians to work toward cost containment in the total expenditures for health care. And it would seem to call for something more than the Voluntary Effort (VE) which has produced some results but nowhere nearly enough.

What is to be done? Two approaches, one new and one not so new, seem necessary. First, physicians' fees or other compensation should be adequate and also clearly justifiable in terms of the economic value of the services rendered. Relatively little attention or study has been given to this. Some improvements are clearly needed. The thinking, problem solving or rendering of professional opinions or advice are not now compensated adequately in terms of their real economic value in health care. The American Society of Internal Medicine (ASIM) calls these "cognitive services" and recognizes that they are rendered by physicians in all specialties. ASIM believes that more incentives for greater use of these cognitive services are needed and that more equitable compensation for them could result in substantial savings in the overall cost of care. Benson Roe has called attention to the need for a more equitable distribution of physicians' fee dollars within the profession.[2] He believes that many surgical fees are unjustifiable especially when they remain high long after a procedure becomes routine or even commonplace. And in another dimension one may ask how justifiable is the substantial compensation above overhead costs that many physicians receive when machines or other health personnel do most of the work for which they are compensated. If physicians' fees or other types of compensation are to be perceived as both adequate and justifiable, the medical profession should address—and where necessary resolve—these sorts of issue, or risk losing control of its finances and perhaps of its destiny.

A second approach that seems necessary is to reassert and strengthen the central role of physicians and of the medical profession in health care in both medical and economic terms—that is, in assuring both quality and economic efficiency in health care. As Fuchs suggests this may not be easy and will require understanding and some compromise in working with administrators and other elements of the health care enterprise, if serious conflicts are to be avoided. However, if his basic premise is correct it is clearly in physicians' own economic self-interest, as well as in the interest of the public, to work in every way possible to restrain the nonphysician portion of health care expenditures whether for hospital care, drugs, administration or whatever.

It is significant, and even a happy prospect for genuine collaboration, that the actual economic self-interest of the great body of physicians seems to coincide so closely with the interests of those in government, business and elsewhere who are seeking ways to hold down the rate of growth of health care expenditures. From all this it is clear that arbitrary reductions in physicians' fees will never accomplish this goal (rather, this is likely to be counterproductive), nor is bureaucratic control of medical practice by administrators in or out of government a likely solution. Rather it is time for physicians and the medical profession to put their own economic house in order and also to reassert and strengthen their central role in patient care and at all other levels of health care, and to take the initiative to assure both quality and economic efficiency in all aspects of care. As Fuchs points out, to do this is in the economic self-interest of both the public and the profession.

—MSMW

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